UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,086	11/29/1999	PASCUAL PEREZ	BET-99/0730	2155

466 7590 02/24/2004

YOUNG & THOMPSON
745 SOUTH 23RD STREET 2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/380,086	PEREZ ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 27-34 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claims 19-26 under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in light of Applicant's cancellation of the new matter.

4. The rejections of claims 19 and 21 under 35 U.S.C. 102(b) as being anticipated by each of Svab et al (1990, Proc. Natl. Acad. Sci. USA 87:8526-8530), Maliga et al (1995, US Patent 5,451,513) and Metz et al (1995, Mol. Breed. 1:309-317) are withdrawn in light of Applicant's amendment to limit equivalent claims to maize, tomato and corn.

5. The rejections of claims 22-24 under 35 U.S.C. 102(b) as being anticipated by each of Jorgensen (1993, US Patent 5,180,873), Mariani et al (US Patent 5,689,041, filed March, 1991) and Fabijanski et al (US Patent 5,728,558, filed July, 1990) are withdrawn in light of Applicant's amendment to limit equivalent claims to therapeutic or prophylactic compounds of human or animal origin.

Claim Rejections - 35 USC § 112

6. Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method for preventing dissemination of any transgene of interest wherein the method uses a maize, rape or tomato plant with cytoplasmic male sterility, any artificial male sterility gene, and/or any transgene encoding a therapeutic or prophylactic compound of human or animal origin. In contrast, the only artificial male sterility genes described in the specification is the glucanase or the barnase gene and the only transgene encoding a therapeutic or prophylactic compound of human or animal origin is the dog gastric lipase gene. The specification does not describe other transgenes encoding a therapeutic or prophylactic compound of human or animal origin or artificial male sterility nor does it describe any maize, rape or tomato plant with cytoplasmic male sterility. Thus, the structural features that distinguish all such nucleic acids and plants from other nucleic acids and plants are not provided.

Because the nucleic acids and plants are not described, the methods of using the nucleic acids and plants to prevent dissemination of a transgene are likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the

> members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

7. Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preventing dissemination of a transgene encoding dog gastric lipase wherein the transgene is on the same vector as the barnase or glucanase male sterility genes, does not reasonably provide enablement for methods for preventing dissemination of any transgene of interest wherein the methods use a maize, rape or tomato plant with cytoplasmic male sterility, any artificial male sterility gene, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 29 May 2003, as applied to claims 22-24 and 26. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

The claims are broadly drawn to methods for preventing dissemination of any transgene of interest wherein the methods use a maize, rape or tomato plant with cytoplasmic male sterility,

any artificial male sterility gene, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin.

The instant specification, however, only provides guidance for construction of plant transformation vectors comprising a gene conferring male sterility, comprising the A9 promoter operably linked to either the glucanase or the barnase gene, a gene encoding dog gastric lipase, and a gene conferring resistance to Basta (examples 1-2); and transformation of the vectors into *Brassica napus* (example 3) and tobacco (example 4). The instant specification also provides guidance for construction of a plant transformation vectors comprising the Ac transposase gene (example 5) and one presumably comprising the A9 promoter operably linked to the glucanase gene and excision sequences (example 6); transformation of the vector of examples 5 and 6 into separate tomato plants (example 7); constructing a vector comprising a Ds element inserted into the Gus gene, transforming this into plants and showing that the plants produced blue spots, *i.e.*, that the Ds element was excised (example 8); and generation of T2 seeds that contain an unidentified transgene (example 9). The instant specification also provides guidance for crossing male sterile plants containing the Ds element and an unknown artificial male sterility gene to plants expressing the Ac transposase (example 10); identification of the excision event in F1 plants by PCR to determine which no longer have the AMS gene - such plants in an unexplained manner also lack the transposase gene but have an undefined gene of interest (example 11); and construction of a plant transformation vectors containing the FLP recombinase (example 12) and the one containing a A9-barnase male sterility gene and a kanamycin resistance gene between FRT recombination sites (example 13).

It is noted that following what exactly was done in the examples and what each vector and plant comprises is very difficult, and in some cases impossible, to determine from the specification.

The instant specification fails to provide guidance for artificial male sterility genes other than the glucanase or the barnase gene, transgenes encoding a therapeutic or prophylactic compound of human or animal origin other than dog gastric lipase, or any maize, rape or tomato plant with cytoplasmic male sterility.

Furthermore, the specification, on pg 2, lines 30-35 states: "Male sterility can also be 'artificial', that is induced by the expression of a gene which confers male sterility (AMS gene) and which is inserted either in the mitochondrial genome (cytoplasmic male sterility) or in the nuclear genome (nuclear male sterility)." The specification does not teach mitochondrial transformation.

Given the claim breath and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for preventing dissemination of any transgene of interest wherein the methods use a maize, rape or tomato plant with cytoplasmic male sterility, any artificial male sterility gene, and/or a transgene encoding any therapeutic or prophylactic compound of human or animal origin.

Applicant urges that production of a plant carrying cytoplasmic male sterility gene can be readily achieved by one of skill in the art using their knowledge and the instant specification and the Office action does not point out why such a person would not be able to do so (response pg 5-6).

This is not found persuasive because the specification does not teach any maize, rape or tomato plant with cytoplasmic male sterility.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

8. Claims 27-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 29 May 2003, as applied to claims 19-26. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

Claims 29 and 30 are indefinite in their recitation of "artificial male sterility (AMS) gene" in lines 6-7. It is unclear what it means for a male sterility gene to be artificial - in what manner is it artificial? It is also unclear how artificial male sterility genes differ from naturally occurring ones, and if naturally occurring ones are excluded.

Applicant urges that the specification on pg 2 teaches that male sterility can be artificial, that is induced by the expression of a gene that confers male sterility (response pg 7-8).

This is not found persuasive because the specification, on pg 2, lines 30-35 only states: "Male sterility can also be 'artificial', that is induced by the expression of a gene which confers male sterility (AMS gene)...." It is unclear how artificial male sterility genes differ from naturally occurring ones, and if naturally occurring ones are excluded.

Claims 28-29 are indefinite in their recitation of "therapeutic or prophylactic compound". Some compounds are therapeutic or prophylactic in some circumstances and toxic or ineffective in others. It is unclear if those compounds are included.

Claim Rejections - 35 USC § 103

9. Claims 29-30 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Halluin et al (US Patent 5,712,135, filed June, 1995) in view of Metz et al (1995, Mol. Breed. 1:309-317) and Welter (WO 98/06861). The rejection is modified from the rejection set forth in the Office action mailed 29 May 2003, as applied to claims 19 and 21-26. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

The claims are drawn to methods of transforming plants with constructs comprising an AMS gene and a collagen gene, with the goal of preventing spread of the collagen gene by pollen.

D'Halluin et al disclose transformation of maize with a male-sterility gene linked to a transgene of interest, the kanamycin resistance gene or the bar gene (column 19, line 47, to column 23, line 36). The kanamycin resistance gene and the bar gene encode compounds that are therapeutic or prophylactic for the plant. D'Halluin et al do not disclose transformation with a gene encoding collagen.

Metz et al teach transformation of cytoplasmically sterile *Brassica oleracea* plants (Table 1). These plants are inherently unable to transmit the transgene via pollen. Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3).

Welter teaches the transformation of plants, including corn, broccoli and tomato, with the gene encoding collagen (claims 1-3, 6-7 and 9-12).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation as taught by D'Halluin et al to transform the plants with a gene encoding collagen, as taught by Welter. One of ordinary skill in the art would have been motivated to do so because of the teachings of Metz et al that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3) and the suggestion of D'Halluin et al to transform the plants with economically important proteins (column 10, lines 43-46).

In a rejection of claims 19 and 21-26 under 35 U.S.C. 103(a) as being unpatentable over each of D'Halluin et al and Metz et al in view of Welter, Applicant urges that Welter was published after the priority date of the instant application, that Metz et al fails to discloses transformation of maize rape or tobacco [sic] and fail to disclose a transgene encoding a therapeutic or prophylactic compound of human or animal origin, and that D'Halluin fails to disclose a transgene encoding a therapeutic or prophylactic compound of human or animal origin (response pg).

This is not found persuasive. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

10. Claims 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metz et al (1995, Mol. Breed. 1:309-317) in view of Vedel et al (1994, Plant Physiol. Biochem. 32:601-618). The rejection is repeated for the reasons of record as set forth in the Office action mailed 29 May 2003, as applied to claims 19-21. Applicant's arguments filed 1 December 2003 have been fully considered but they are not persuasive.

The claims are drawn to methods of transforming CMS *B napus* and maize plants with constructs comprising a transgene, with the goal of preventing spread of the gene by pollen.

Metz et al teach transformation of cytoplasmically sterile *Brassica oleracea* plants (Table 1). These plants are inherently unable to transmit the transgene via pollen. Broccoli would be cultivated for seed production for planting. As Metz et al teach all the method steps of the instant claims, Metz at al inherently teach the instantly claimed method. Additionally, Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3). The Bt gene encodes a compound that would be therapeutic or prophylactic for the plant.

Metz et al do not disclose CMS *B napus* or maize plants.

Vedel et al teach CMS *B napus* and maize plants (Table 3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transforming CMS plants with constructs comprising a transgene, with the goal of preventing spread of the gene by pollen, as taught by Metz et al to CMS *B napus* and maize plants as described in Vedel et al. One of ordinary skill in the art

would have been motivated to do so because Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3).

Applicant urges that Metz et al is concerned with the protection of plants against plant pests and Vedel discusses different types of male sterility.

This is not found persuasive. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant urges that Metz et al are not concerned with the prevention of transgene dissemination and do not pertain to the same technical area as Vedel et al; thus, one of skill in the art would lack a motivation and reasonable expectation of success in combining and modifying the teachings of Vedel et al and Metz et al to obtain the claimed invention (response pg 13-14).

This is not found persuasive. Metz et al are concerned with the prevention of transgene dissemination; they teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3). Metz et al use CMS plants, and are thus in the same technical area as Vedel et al, who teach CMS plants. One of skill in the art would thus have a strong a motivation and every expectation of success in combining and modifying the teachings of Vedel et al and Metz et al to obtain the claimed invention.

11. Claims 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metz et al (1995, Mol. Breed. 1:309-317) in view of Vedel et al (1994, Plant Physiol. Biochem. 32:601-618) as applied to claims 27-28 above, and further in view of each of Welter (WO 98/06861) and Lenee et al (US 6,573,431, filed April 1996).

The claims are drawn to methods of transforming CMS *B napus* and maize plants with constructs encoding collagen or dog gastric lipase, with the goal of preventing spread of the constructs by pollen.

The teachings of Metz et al in view of Vedel et al are discussed above. Metz et al in view of Vedel et al do not disclose a gene encoding collagen as that transgene.

Welter teaches the transformation of plants, including corn, broccoli and tomato, with a gene encoding collagen (claims 1-3, 6-7 and 9-12).

Lenee et al teach transformation of plants, including corn and rape, with a gene encoding dog gastric lipase (claim 10).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transforming CMS *B napus* and maize plants with constructs comprising a transgene as taught by Metz et al in view of Vedel et al, to transform the plants with a gene encoding collagen, as taught by Welter. One of ordinary skill in the art would have been motivated to do so because of the teachings of Metz et al that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3) and because escape of genes encoding mammalian proteins is of great concern in the general public.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 18, 2004

ANNE KUBELIK
PATENT EXAMINER

ANNE KUBELIK
PATENT EXAMINER